Claims

1. A ligand to a member of the TNF/NGF receptor family which binds either to the region of the fourth cysteine rich domain of such a receptor, or to the region between it and the cell membrane.

2. A ligand according to claim 1, wherein the fourth cysteine rich domain includes the amino acid sequence of about pro-141 to thr-179 in the p75 TNF-R, or a corresponding region in another member of the TNF/NGF receptor family.

3. A ligand according to claim 2, wherein the fourth cysteine rich domain includes the amino acid sequence of about cys-163 to pro-141 in the p75 TNF-R, or a corresponding region in another member of the TNF/NGF receptor family.

4. A ligand according to claim 1, wherein the region between the fourth cysteine rich domain and the cell membrane includes about thr-179 to the end of the extracellular domain of the p75 TNF-R, or a corresponding region in another member of the TNF/NGF receptor family.

5. A ligand according to any one of the preceding claims, which comprises a ligand to a TNF-R.

6. A ligand according to claim 5, wherein the receptor is the p75 TNF-R.

7. A ligand according to any one of claims 1 to 3, including the amino acid sequence for the CDR region of the heavy chain of monoclonal antibody no. 67 and/or its light chain.

8. A ligand according to any one of claims 1 to 3, including the amino acid sequence for the CDR region of the heavy chain of monoclonal antibody no. 81 and/or its light chain.

9. A ligand according to any one of claims 1 to 3, including the amino acid sequence of an antibody raised against the fourth cysteine rich domain of a member of the TNF/NGF receptor family.

10. A ligand according to any one of claims 1 to 9, comprising a protein.

11. A ligand according to any one of claims 1 to 9, comprising a peptide.

12. A ligand according to any one of claims 1 to 9, the three-dimensional structure of which is similar as a pharmacophore to the three-dimensional structure of the protein or peptide as claimed in claims 10 and 11, and being capable of inhibiting the effect of TNF but not its binding to the TNF-R.

13. A DNA molecule encoding a ligand according to any one of claims 1 to 12, capable of expressing such a ligand.

14. A DNA molecule hybridizing to a DNA molecule according to claim 13 and capable of expressing a ligand according to any one of claims 1 to 12.

15. A replicable expression vehicle comprising a DNA molecule according to claim 13 or 14, and capable, in a transformant host cell, of expressing a ligand according to any one of claims 1 to 12.

16. A host cell transformed with the replicable expression vehicle of claim 15.

17. A prokaryotic host cell according to claim 16.

18. A eukaryotic host cell according to claim 16.

19. A process for the production of a recombinant ligand according to claim 1, comprising culturing a transformed host cell according to claim 16 and recovering the recombinant ligand.

20. A pharmaceutical composition comprising a ligand according to claim 1.

1806 21. An anti-idiotypic antibody to a ligand according to any one of claims 1 to 12, capable of inhibiting the effect of TNF, but not its binding to the TNF-R.

22. Use of a ligand according to any one of claims 1 to 12 for increasing the inhibitory effect of a soluble receptor of the TNF/NGF receptor family.

23. Use of soluble mutated receptor forms of the TNF/NGF receptor family in which the region corresponding to the group 67 epitope or the anti-stalk region has the conformation occurring when antibodies of the 67 group or the anti-stalk region in the p75-R bind to it, as a more effective inhibitor than the natural form for the function of the respective ligand.